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Applicants	:	Keiji SHIMIZU et al.
Filed	:	March 26, 2004
For	:	ILLUMINATION DEVICE FOR MICROSCOPE
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Examiner	:	Lee A. FINEMAN
Docket No.	:	04200/LH
Confirmation No.	:	8009
Customer No.	:	01933

DECLARATION UNDER 37 CFR 1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

S I R :

We, the undersigned inventors of the above-identified application, hereby declare that:

1. The primary reference in the 35 USC 103 rejection in the July 18, 2007 Office Action is US 2003/0063376. US 2003/0063376 has a U.S. filing date of September 23, 2002 and a U.S. publication date of April 3, 2003. The corresponding Japanese publication is JP 2003-107361, which was published on April 9, 2003.

The above-identified patent application has a U.S. filing date of March 26, 2004 and a priority date of April 4, 2003.

Since US 2003/0063376 was not published more than one year before the U.S. filing date of the above-identified patent application, US 2003/0063376 is not a reference against the above-identified patent application under 35 USC 102(b).

US 2003/0063376 could qualify as a reference against the above-identified patent application under 35 USC 102(a).

2. This DECLARATION is being filed to provide evidence of the completion of the invention of the above-identified patent application in order to remove US 2003/0063376 as a reference.

3. Prior to April 3, 2003, the invention of the above-identified patent application was conceived and reduced to practice in Japan, a WTO country, as evidenced by the document submitted herewith and as explained below.

4. Attached to this DECLARATION is a facsimile letter and an enclosure (entitled "Written Proposal of Invention") from Mr. Makoto Shigehara of OLYMPUS CORPORATION, the assignee of the above-identified patent application, to Mr. Ihara of SUZUYE & SUZUYE, a patent law firm in Japan. The "Written Proposal of Invention" is a disclosure of our invention and fully supports the claims of the above-identified patent application. Also attached to this DECLARATION are an English-language translation of Mr. Shigehara's facsimile letter and an English-language translation of the "Written Proposal of Invention", pp. 1 to 25.

5. Further attached to this DECLARATION is a paper entitled "Support for Claims in English Language Written Proposal of Invention and in the Drawings in the Japanese Language Written Proposal of Invention," which describes where in the enclosed documents the features in applicants' claims are supported.

6. From the attached documents, it can be seen that the invention of the above-identified patent application was completed at least prior to April 3, 2003.

7. Each of the dates deleted from the attached documents is prior to April 3, 2003.

We hereby declare that all statements made herein of our own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001, of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: Oct. 5, 2007 By: Keiji Shimizu
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(開発受付番号: 35B109　　受付者:　　日付:　　)

知的財産法務部受付番号	受付者	知的財産法務部受付日付印

発明提案書

1．発明の名称（仮）
顕微鏡用照明装置

2．請求の範囲案 (Novel features include the following)

1）対物レンズと、視野絞り投影レンズと、標本共役位置かつ対物レンズで形成される光軸に垂直に置かれたＤＭＤ素子と、該ＤＭＤの光軸上の前後少なくとも１方に置かれた反射部材と、照明光路中に置かれ照明光路を遮光するシャッタと、該ＤＭＤ素子及び該シャッタを制御するためのコントローラーとを有することを特徴とする顕微鏡。

2）対物レンズと、視野絞り投影レンズと、標本共役位置かつ対物レンズで形成される光軸に垂直に置かれたＤＭＤ素子と、該ＤＭＤの光軸上の前後少なくとも１方に置かれた反射部材と、ＬＥＤ光源と、該ＤＭＤ素子及び該ＬＥＤ光源を制御するためのコントローラーとを有することを特徴とする顕微鏡。

3）対物レンズと、視野絞り投影レンズと、標本共役位置かつ対物レンズで形成される光軸に垂直に置かれたＤＭＤ素子と、該ＤＭＤのオン／オフに対応した２つの光軸上の後に置かれた各々少なくとも１つの反射部材と、該2つの光軸上に置かれ照明光路を遮光するシャッタと、該ＤＭＤ素子及び該シャッタを制御するためのコントローラーとを有することを特徴とする顕微鏡。

4）照明する際に、該ＤＭＤ素子制御後に該シャッタを開く制御を連動させることを特徴とする請求項１または３記載の顕微鏡。

5）照明する際に、該ＤＭＤ素子制御後に該ＬＥＤを点灯させる制御を連動させることを特徴とする請求項２記載の顕微鏡。

3．産業上の利用分野、従来の技術

（当社技術）１．特願2001-304123

（他社技術）１．特開平7-134250 （ニコン）　２．特表2000-502472（ライカ）

本発明は顕微鏡、特に蛍光顕微鏡の照明装置に関するものである。
特願2001-304123に示すように、ケーラー照明を持った顕微鏡用照明装置においてＤＭＤ素子を標本共役位置に配置した照明装置が提案されている。

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４．発明が解決しようとする課題（発明の目的）

一般的にＤＭＤ素子はその構造上マイクロミラー保護の為に保護ガラスが必要であり、保護ガラスはマイクロミラー近傍に配置されている。また微小ではあるが、マイクロミラー間の隙間部が存在する。
そしてＤＭＤ素子に照明光が入射した際に、これら保護ガラスやマイクロミラーの隙間部からの反射光がマイクロミラーの制御によらない迷光として微少であるが存在する。
この状態で照明光学系として使用すると、例えばマイクロミラーの制御により標本の一部分だけに照明光を当てようとしたばあいに、微弱ではあるが指定範囲以外にも照明光が照射されてしまう。
範囲指定の目的が標本保護のために指定箇所以外の標本に余分な光りを当てない場合であれば、標本全体に微弱な照明光が照射されいるため、標本保護の効果が薄れる。
また、範囲指定の目的がFRAPなどによる部分的な蛍光ラベルの褪色だった場合は、迷光により標本全体に常に褪色用の照明光が照射されているため、照射時間が長い場合等は特に少なからず標本全体に褪色が起こり、実際の褪色制御後に標本全体を蛍光観察し拡散を観察する場合に、コントラストが落ちる可能性がある。

５．課題を解決するための手段および作用

本発明は照明光路中に、ＤＭＤ素子の制御と連動して開閉するシャッタを装備し、コンピュータからのＤＭＤ素子の制御に合わせてシャッタを開閉することで、ＤＭＤ素子の制御中以外は照明光が標本に照射されないようにする。
また、ＤＭＤ素子の制御と連動してＬＥＤ光源をオン／オフすることで、ＤＭＤ素子の制御中以外は照明光が標本に照射されないようにする。

６．発明の実施の形態

（第１実施例）

図１は本発明の第1実施例を示す図であって、顕微鏡光学系の概念的光学図を示す。
１は水銀ランプの如き光源。２はコレクタレンズ。３は反射ミラー。４はＤＭＤ素子。５は視野絞り投影レンズ。６は光源からの照明光を選択的に透過する励起フィルタ。７はダイクロイックミラー。８は対物レンズ。９は蛍光標本。10は標本９からの蛍光を選択的に透過する吸収フィルタ。11が結像レンズ。12はプリズム。13は接眼レンズ。14は対物レンズ８によってなる観察光軸で15は観察光軸14がダイクロイックミラー７によって反射された照明光軸である。16は照明光を遮光できる高速シャッタ。16'は該高速シャッタ16の別のい配置例。17は観察象を取得するためのカメラ。18は画像処理やＤＭＤ素子、シャッタの制御をコントロールするためのコンピュータ。19はコンピュータに接続されたモニタ。20はコンピュータ18からの制御によりＤＭＤ素子及びシャッタを駆動制御するための駆動制御部である。
ＤＭＤ素子４は照明光軸15に対し垂直になるように配置されており、観察光軸14に対し垂直に投影されるようになっている。またＤＭＤ素子4は微小ミラー４a、４b…からなり（２つの素子だけが図示されている。実際には微小ミラーは例えば1024×768個の配列になっている。）、それぞれの垂線に対し予め決められた傾斜角度±αの安定した固定状態に個別に傾斜させることができる。傾斜角度αは使用されるＤＭＤに依存するが、例えばα＝10°である。また各微小ミラーはＤＭＤに依存する予め決められた面積を有するが、例えば20μm以下の方形である。各微小ミラーは十マイクロ秒オーダーの応答速度で固定状態間で切換ることができる。固定状態は光源１からの光りを照明光軸15方向に導く状態が“オン”でもう一方の光軸21方向に導く

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状態を“オフ”と呼ぶ。
投影レンズ５の焦点位置は対物レンズ８の瞳位置およびＤＭＤ素子４の面上になるように配置されている。
以上にように構成された装置に対し、その作用を説明する。
光源１からでた光りは、コレクタレンズ２により集光され、シャッタ16が開いている場合には反射ミラー３で反射されＤＭＤ４へ導かれる。ＤＭＤ４上の微小ミラーがオンになっている（例えば4a）箇所は照明光軸15方向へ反射され投影レンズ５へ導かれる。ＤＭＤ４上の微小ミラーがオフになっている（例えば4b）箇所は退避光軸21方向へ反射され、照明として使用されない。投影レンズ５に導かれた光は励起フィルタ６により標本９の蛍光物質を励起するのに適当な光りに選択され、ダイクロイックミラー７により反射され、対物レンズ８により標本９に照射される標本９から発した蛍光は対物レンズ８により集光され、ダイクロイックミラー７を透過し、吸収フィルタ10により蛍光が選択的に透過され、結像レンズ11により結像され、プリズム12により偏向され、接眼レンズ13により観察される。ここでＤＭＤ素子４の各微小ミラー像は投影レンズ５と対物レンズ８により標本ピント面に結像される。微小ミラー4aの像は反射光が標本面まで導かれているため明るく投影される。微小ミラー4bの像は反射光が標本面に導かれないために、真暗に投影される。つまり標本上ではＤＭＤ素子４の各微小ミラー像はそのオン／オフの状態により明暗として投影されるため、明の部分のみを照明している状態となる。よってＤＭＤの各微小ミラーのオン／オフ制御によって、部分的な照明が可能となる。
例えば図２ｂはＤＭＤ素子４の制御状態を示す図で、図２ａに示すようなモニタ１９の画面上で指定された領域31に対応する微小ミラーのみがオンの状態になっている。図２ｃは図２ｂが標本面に投影された状態を示すもので、領域33はＤＭＤ素子４上の領域３２に対応しており、観察視野３４に対して、領域３３の部分のみが明るく照明されている状態となる。また、ＤＭＤを制御することによって領域３３ａ、３３ｂ、３３ｃをそれぞれ単独で照明することも可能であるし、高速に順次切換えて照明することも可能である。例として領域を3箇所で示したが、ＤＭＤ素子４上の微小ミラーを最小単位とした制御で可能であれば領域数に制限は無く、その大きさや形状も任意に変更できる。
しかしながらここでＤＭＤ素子４には保護ガラス22や微小ミラーの隙間23が存在する。この保護ガラス22や隙間23から微小ながら反射光24が反射する。この24は正規の照明15には一致しないが、退避光軸21ほどの角度はつかないため、場合によっては光軸15に近傍に反射され投影レンズ５に導かれることで標本9の意図しない位置へ導かれることがある。例えば前述のように領域31の微小ミラーをオンにし、領域33のみを照明しようとした場合でも、前記保護ガラス22や隙間23からの反射光が観察視野32の領域33以外の部分も照明してしまう。
該保護ガラス22による反射光や隙間23からの反射光は正規の微小ミラーオン時の反射光に比べて極めて微弱であるため、多くの場合は問題とはならない。しかし、照明光の強度が高い場合や照明照射時間が長い場合などは標本への影響を考慮しなければならない。
例えば一般的な蛍光観察で観察する場合にシャーレ内に培養された複数の細胞のうち、一つの細胞のみを選びたい場合は、細胞に相当する一部分（例えば領域33a）のみを照明することになるが、前記保護ガラス22や隙間23からの迷光により観察対象以外の細胞へも微弱な照明光が当たっているため、しらずに長時間の観察などを行なうと、観察対象以外の細胞が褪色したり、場合によっては弱ったりすることがある。
さらに、蛍光観察時に視野内を部分的に褪色させ、その復帰状態を観察することで、細胞内の物質移動を観察する手段であるＦＲＡＰ(Fluorescence Recovery after Photobleaching)観察などでは、ＤＭＤ素子４を制御することで、褪色させる範囲（位置、形状、大きさ）を指定し、照明光を一定時間照射し部分的に蛍光を褪色させる。その後ＤＭＤ素子４の視野32に対応する範囲の微小ミラーを全てオンにし、蛍光観察を行い、褪色した部分への周囲の蛍光色素の拡散を観察する。この時前述した迷光の影響で、光源を点灯させている間は褪色範囲以外も含む前標本範囲に照明光が照射されていることになり、標本全体で褪色が進む。褪色させる照明光は観察に対して強力な照明光を照射するため、微弱な迷光であっても褪色が無視できない場合がある。指定範囲以外が褪色すると、観察視野32を蛍光観察する際に褪色領域と蛍光領域の格差が小さくなり拡散のコントラストが悪くなるので、観察しにくくなるばかりか場合によっては結果が得られない場合もある。
本実施例では照明光路中に制御可能なシャッタ16を配置している。ＤＭＤ素子４の制御に合わせシャッタ16を連動させて制御することで、必要時間外の照明光を遮断し、前述した迷光による照明光の標本照射を最大限にカットすることが可能になる。

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例えばＦＲＡＰ観察の流れの一例を下記に示す。

・観察開始（スイッチON）
・シャッタ閉
・対象サンプルの所望の部位が確認できる観察法（蛍光、位相差等）にセット（以下蛍光で説明）
・標本セット
・準備観察スタート支持
　・微小ミラー（ＤＭＤ）をフルオン
　・シャッタ開
　・カメラ（CCD等）にて撮像
　・撮像終了
　・シャッタ閉
　・画像の保存
・準備観察終了
・パラメータ指定開始支持
　・撮像したサンプル像をモニターに表示（画像呼出）
　・モニター上で確認しながら、照明光を照射する領域を指定（領域指定）複数可
　　（指定方法はフリーハンド指定、予め区分けしたブロック毎指定等任意）
　・指定した領域をコンピュータに保存（領域保存）
　・保存データを呼び出しコンピュータで褪色照射領域に対応する微小ミラーを選択（領域呼出）
　・褪色照明照射時間を選択
　・領域保存データを呼び出し、観察範囲を指定
　・観察時間を指定
・パラメータ指定終了
・アプリケーションスタート支持
　・褪色照明
　　・選択した褪色領域微小ミラーを駆動制御部へ出力
　　・選択した褪色照明照射時間を駆動制御部へ出力
　　・駆動制御部が選択された微小ミラーをオン
　　・シャッタ開
　　・褪色照明照射
　　・照射時間終了
　　・シャッタ閉
　・経過観察
　　・観察範囲領域の微小ミラーを駆動制御部へ出力
　　・駆動制御部が選択された微小ミラーをオン
　　・シャッタ開
　　・カメラにて撮像
　　・観察指定時間終了
　　・シャッタ閉
・アプリケーション終了
・標本を取外す
・観察終了

上記ＦＲＡＰ観察の流れの中で、準備観察及びアプリケーションは予め組まれたコンピュータのソフトにより支持による開始から終了までは自動的に流れるようになっている。
ここで標本に照明光が照射されているのは下線部のシャッタ開からシャッタ閉の間の時間のみであり、観察等に必要な最小限の時間だけである。
シャッタが存在しない場合は標本への照明光の照射制御はＤＭＤの微小ミラーをすべてオフにすることで行われ、下線部の照射時間以外は全てオフにすることで標本照明はされていないこととなっている。しかし前

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述した通り、保護ガラス22や微小ミラー隙間23からの微弱な照明光が、上記流れの標本セットから標本取外しの間に渡りずべての時間標本に照射されていることになる。特に準備観察からアプリケーション開始までに必要なパラメータ設定時間は人為的作業によるため時間がかかり、その間の照射で標本へダメージを与えることになるばかりか、標本全体の蛍光褪色が生じるため後のアプリケーションでのS/N比劣化への影響もある。
また上記の流れのように準備観察、アプリケーション観察ではソフトにより自動的に流れるように制御し、ＤＭＤの微小ミラー設定後にシャッタを開くように連動制御することで、標本への照明照射時間は必要最小限にすることができる。
以上のように本発明によれば、迷光による標本への余分な照明照射を最大限抑えられるので、ＤＭＤの特性を活かした標本の褪色や標本へのダメージが少なく、コントラストの良い、良好な観察が可能となる。

本実施例ではシャッタ16の位置をＤＭＤ素子４より光源１側に配置しているが、破線で示す16'のごとくＤＭＤ素子４より投影レンズ５側の光軸15上に配置されてもなんら問題ない。

（第２実施例）

図３は第２実施例を示す図で、第１実施例と同様の機能を持つ構成は同番号で示し,説明を省略する。
４１はＬＥＤ光源でＬＥＤ駆動制御部からのコントロールにより高速にオン（点灯）／オフ（消灯）が可能である。ＤＭＤ素子４の制御に合わせＬＥＤ４１のオン／オフを連動させて制御することで、必要時間外の照明光を遮断し、前述した迷光による照明光の標本照射を最大限にカットすることが可能になる。
第１実施例と同様にＦＲＡＰ観察を行なう場合の流れは以下の通りである。

- ・観察開始（スイッチON）
- ・ＬＥＤ光源オフ（確認）
- ・対象サンプルの所望の部位が確認できる観察法（蛍光、位相差等）にセット（以下蛍光で説明）
- ・標本セット
- ・準備観察スタート支持
  - ・微小ミラー（ＤＭＤ）をフルオン
  - ・ＬＥＤ光源オン
  - ・カメラ（CCD等）にて撮像
  - ・撮像終了
  - ・ＬＥＤ光源オフ
  - ・画像の保存
- ・準備観察終了
- ・パラメータ指定開始支持
  - ・撮像したサンプル像をモニターに表示（画像呼出）
  - ・モニター上で確認しながら、照明光を照射する領域を指定（領域指定）複数可
    （指定方法はフリーハンド指定、予め区分けしたブロック毎指定等任意）
  - ・指定した領域をコンピュータに保存（領域保存）
  - ・保存データを呼び出しコンピュータで褪色照射領域に対応する微小ミラーを選択（領域呼出）
  - ・褪色照明照射時間を選択
  - ・領域保存データを呼び出し、観察範囲を指定
  - ・観察時間を指定
- ・パラメータ指定終了
- ・アプリケーションスタート支持
  - ・褪色照明
    - ・選択した褪色領域微小ミラーを駆動制御部へ出力
    - ・選択した褪色照明照射時間を駆動制御部へ出力
    - ・駆動制御部が選択された微小ミラーをオン

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・ＬＥＤ光源オン
・褪色照明照射
・照射時間終了
・ＬＥＤ光源オフ
・経過観察
・観察範囲領域の微小ミラーを駆動制御部へ出力
・駆動制御部が選択された微小ミラーをオン
・ＬＥＤ光源オン
・カメラにて撮像
・観察指定時間終了
・ＬＥＤ光源オフ
・アプリケーション終了
・標本を取外す
・観察終了

上記ＦＲＡＰ観察の流れの中で、準備観察及びアプリケーションは予め組まれたコンピュータのソフトにより支持による開始から終了までは自動的に流れるようになっている。
ここで標本に照明光が照射されているのは下線部のＬＥＤ光源オンからＬＥＤ光源オフの間の時間のみであり、観察等に必要な最小限の時間だけである。
また上記の流れのように準備観察、アプリケーション観察ではソフトにより自動的に流れるように制御し、ＤＭＤの微小ミラー設定後にＬＥＤ光源をオンするように制御することで、標本への照明照射時間は必要最小限にすることができる。
以上のように本発明によれば、迷光による標本への余分な照明照射を最大限抑えられるので、ＤＭＤの特性を活かした標本の褪色や標本へのダメージが少なく、コントラストの良い、良好な観察が可能となる。
またＬＥＤのオン／オフは一般的に数百ナノ秒オーダーで可能なため、数十ナノ秒で可能なＤＭＤの高速切換えと合わせて照明箇所の切換えが極めて高速におこなえるため、褪色照明から経過観察に移る際の試料の変化に対してタイムラグの影響の少ない観察が可能となる。

（第３実施例）

図４は第３実施例を示す図で、第１、第２実施例と同じ構成、作用の部分は同じ番号で示し、説明を省略する。
51、51は水銀ランプの如き光源。53、54はコレクタレンズ。55、56は反射ミラー。57、58はそのぞれ特性の異なる励起フィルタ。59はＤＭＤ素子４の微小ミラーがオンの4aの状態での反射光軸。60はＤＭＤ素子４の微小ミラーがオフの4bの状態での反射光軸。61、62は照明光を遮断できる高速シャッタである。である。
以上のように構成された顕微鏡で作用を説明する。
光源51からでた光は、コレクタレンズ53により集光され、シャッタ61が開いている場合には励起フィルタ57により選択的に透過し、反射ミラー55で反射されＤＭＤ４へ導かれる。ＤＭＤ４上の微小ミラーがオンになっている状態4aの箇所は照明光軸15方向へ反射され投影レンズ５へ導かれる。ＤＭＤ４上の微小ミラーがオフになっている状態4bでは退避光軸方向へ反射され、照明として使用されない。同様に光源52からでた光は、コレクタレンズ54により集光され、シャッタ62が開いている場合には励起フィルタ58により選択的に透過し、反射ミラー56で反射されＤＭＤ４へ導かれる。ＤＭＤ４上の微小ミラーがオフになっている状態4bの箇所は照明光軸15方向へ反射され投影レンズ５へ導かれる。ＤＭＤ４上の微小ミラーがオンになっている状態4aでは退避光軸方向へ反射され、照明として使用されない。
ここで第1及び第2実施例で説明したＦＲＡＰ観察では、なるべく短時間での褪色を行うために、褪色の際に用いる照明の波長を短くして（例えばＵＶにして）エネルギーを増したり、観察用とは異なる高出力の光源を使用してエネルギーを増したりすることが行われる。つまり図４の光源51及び励起フィルタ57は観察に適した特性に設定し、光源52及び励起フィルタ58は標本褪色用に適した特性に設定される。このように設定さ

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証人(READ AND UNDERSTOOD BY:)	日付	証人(READ AND UNDERSTOOD BY:)	日付

れた装置において、第1実施例同様ＦＲＡＰ観察の流れの一例を示す。

・観察開始（スイッチON）
・シャッタ61，62閉
・対象サンプルの所望の部位が確認できる観察法（蛍光、位相差等）にセット（以下蛍光で説明）
・標本セット
・準備観察スタート支持
　・微小ミラー（ＤＭＤ）をフルオン
　・シャッタ61開
　・カメラ（CCD等）にて撮像
　・撮像終了
　・シャッタ61閉
　・画像の保存
・準備観察終了
・パラメータ指定開始支持
　・撮像したサンプル像をモニターに表示（画像呼出）
　・モニター上で確認しながら、照明光を照射する領域を指定（領域指定）複数可
　　（指定方法はフリーハンド指定、予め区分けしたブロック毎指定等任意）
　・指定した領域をコンピュータに保存（領域保存）
　・保存データを呼び出しコンピュータで褪色照射領域に対応する微小ミラーを選択（領域呼出）
　・褪色照明照射時間を選択
　・領域保存データを呼び出し、観察範囲を指定
　・観察時間を指定
・パラメータ指定終了
・アプリケーションスタート支持
　・褪色照明
　　・選択した褪色領域微小ミラーを駆動制御部へ出力
　　・選択した褪色照明照射時間を駆動制御部へ出力
　　・駆動制御部が選択された微小ミラーをオフ（他オン）
　　・シャッタ62開
　　・褪色照明照射
　　・照射時間終了
　　・シャッタ62閉
　・経過観察
　　・観察範囲領域の微小ミラーを駆動制御部へ出力
　　・駆動制御部が選択された微小ミラーをオン（他オフ）
　　・シャッタ61開
　　・カメラにて撮像
　　・観察指定時間終了
　　・シャッタ61閉
・アプリケーション終了
・標本を取外す
・観察終了

上記ＦＲＡＰ観察の流れの中で、準備観察及びアプリケーションは予め組まれたコンピュータのソフトにより支持による開始から終了までは自動的に流れるようになっている。
ここで標本に照明光が照射されているのは下線部のシャッタ開からシャッタ閉の間の時間のみであり、観察等に必要な最小限の時間だけである。
本実施例の構成ではシャッタ61及び62が存在しない場合は常にどちらかの光源の照明が標本に照射されていることになり、標本へのダメージや蛍光褪色は避けられない。

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以上のように本発明によれば、異なる光源や波長により、それぞれの特性を活かした効率の良い照明が可能で、且つ迷光による標本への余分な照明照射を最大限抑えられるので、ＤＭＤの特性を活かした標本の褪色や標本へのダメージが少なく、コントラストの良い、良好な観察が可能となる。

（変形例）

第3実施例ではＦＲＡＰ観察について主に説明したが、励起フィルタ57、58の特性を変えた2色照明による観察も当然可能である。

この時、例えば図２の視野34内のＤＭＤ素子４がオンになっている状態に対応する任意領域33は光源51からの照明光で照明され、ＤＭＤ素子４がオフになっている状態に対応する領域33以外は光源52からの照明光で照明される。この時励起フィルタ57と58を異なる波長帯域のバンドパスフィルタにしてやることで、領域33とそれ以外を異なる波長で照明することができる。

この様な構成でケージド蛍光試薬による観察を行う場合。領域33をケージド解除の波長で照明し、領域33以外を解除後の蛍光観察の波長で照明することで、まさに解除しながら同時にタイムラグ無しに拡散の様子を観察することができる。

（変形例２）

第3実施例では、光源51,52及びシャッタ57、58を用いたが、片側光路例えば光軸59側の光源51をＬＥＤ光源にしてシャッタ61を廃止し、シャッタ61の開閉制御に変えてＬＥＤ光源のオンオフを制御するようにすることで、第3実施例と全く同じ効果が得られる。

もちろん光源51、52を両方ＬＥＤ光源にし、シャッタ61、61を廃止してやることも当然可能である。

７．発明の効果

請求項１：実施例１
請求項２：実施例２
請求項３：実施例３

発明者 (DISCLOSED BY INVENTOR:)	日付	発明者 (DISCLOSED BY INVENTOR:)	日付
証人(READ AND UNDERSTOOD BY:)	日付	証人(READ AND UNDERSTOOD BY:)	日付

図1

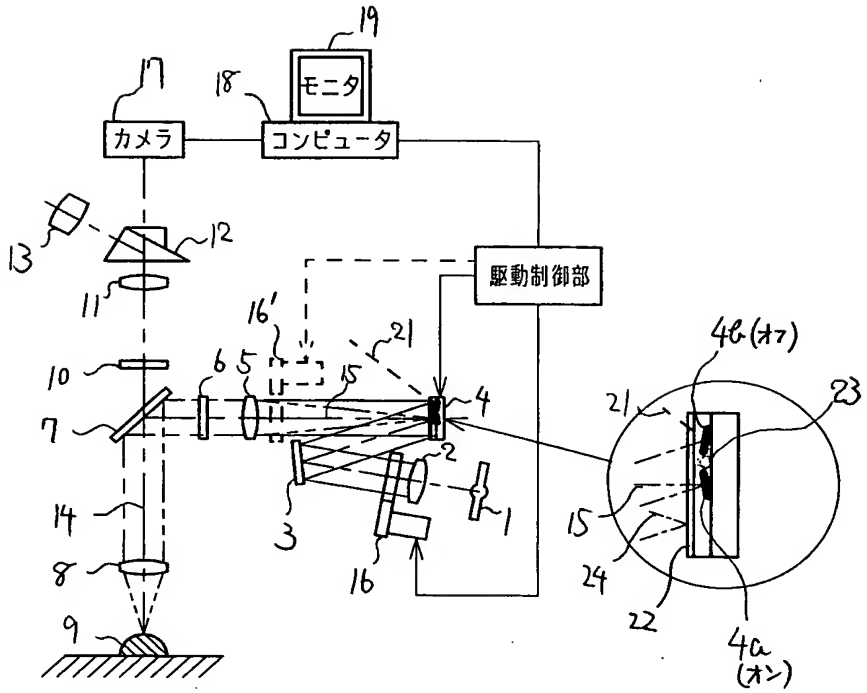

19
モニタ
17
18
カメラ
コンピュータ
13
12
11
駆動制御部
16'
21
4a(オフ)
10
6
5
15
4
21
23
7
2
14
3
1
15
8
16
24
9
22
4a
(オン)

図2

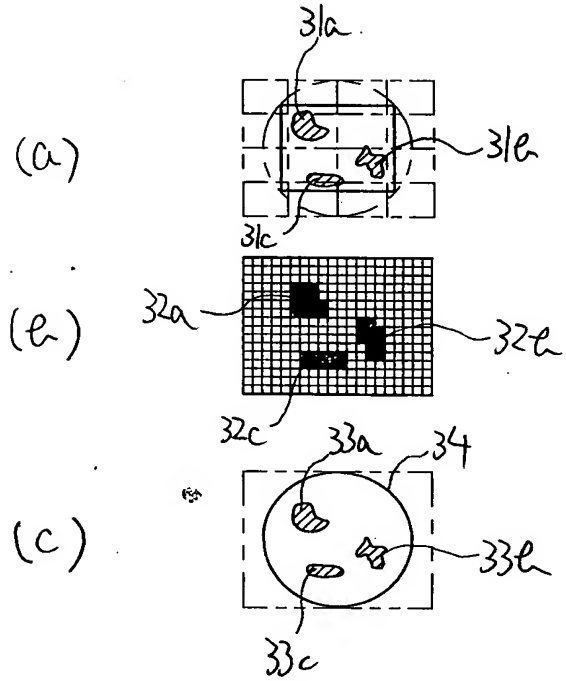

31a
(a)
31b
31c
(b)
32a
32b
32c
33a
34
(c)
33b
33c

図3

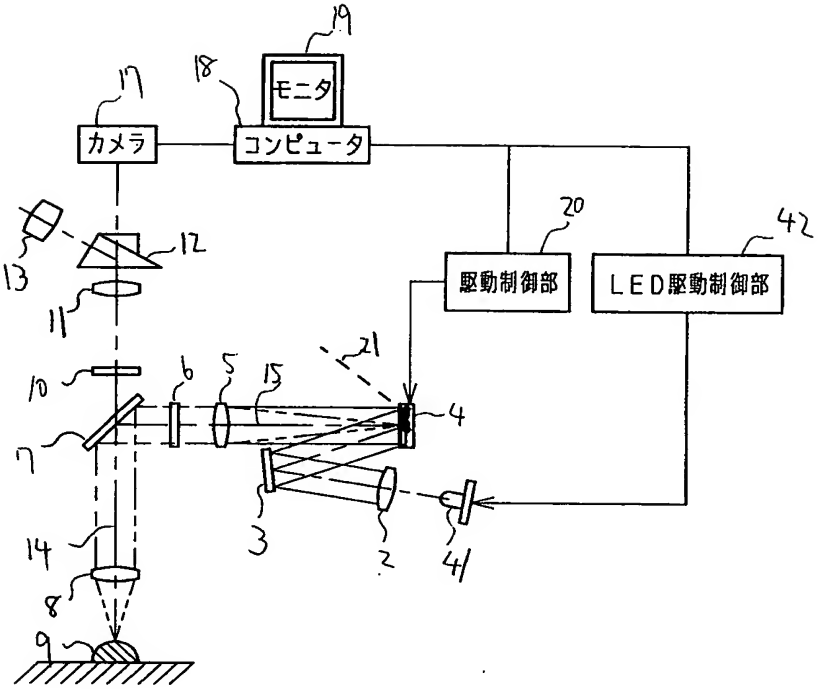
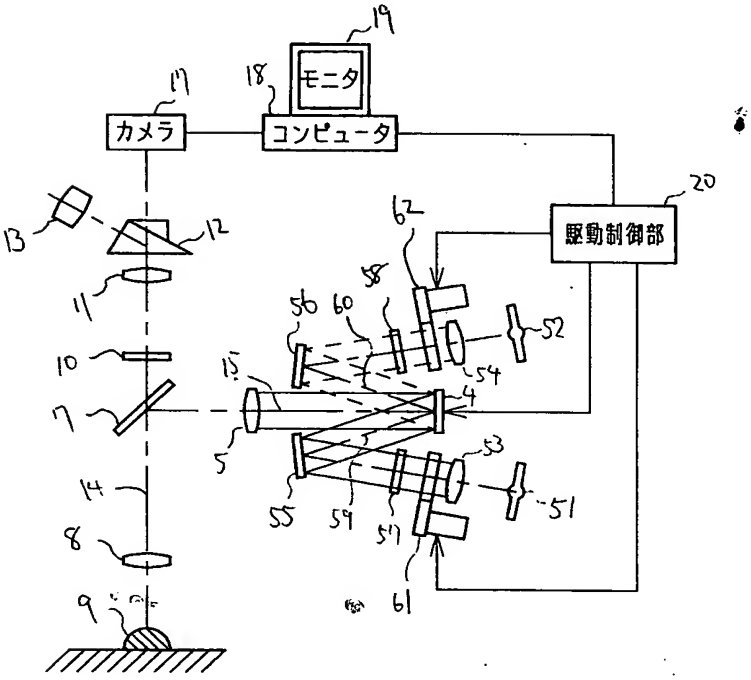

19
モニタ
18
17
カメラ
コンピュータ
20
42
駆動制御部
LED駆動制御部
13
12
11
21
10
6
5
15
4
7
3
2
41
14
8
9

図4


19
モニタ
18
17
カメラ
コンピュータ
20
駆動制御部
13
12
11
62
58
56
60
52
10
15
54
4
7
5
53
14
55
59
57
51
8
9
61

Facsimile Letter

Date: [Redacted]

Number of pages including cover page: 11

To: Mr. Ihara, SUZUYE & SUZUYE, Division 3

FAX No. (03) 3512-6771

From: Makoto Shigehara, Olympus Corporation, Medical Business Division, 2951, Ishikawa-cho, Hachioji-shi, Tokyo, 192

FAX: 0426-42-2114 TEL: 42-2334

Subject: case of sending written proposal of urgent application (35B109)

Dear Sirs,

I am glad to hear that things are going well for you.

I am sending a written proposal of a matter requested by you by phone yesterday.

I send a new written proposal because there is an addition thereto. If you can understand contents (invention from special inspection of microscope) with this written proposal, you may form a specification draft without discussion.

I hope for application completion at [Redacted]

Your cooperation is greatly appreciated.

Yours sincerely

Written Proposal of Invention

1. Title of the Invention (temporary)

ILLUMINATION DEVICE FOR MICROSCOPE

2. Claim draft (Novel features include the following)

1) A microscope comprising:

an objective;

a field stop projection lens;

a DMD (Digital Micromirror Device) element placed perpendicularly to a specimen conjugation position and an optical axis formed with the objective;

a reflection member placed in at least one of the front and the rear on the optical axis of the DMD;

a shutter placed in rays of an illumination light path and shielding the rays of the illumination light path; and

a controller to control the DMD element and the shutter.

2) A microscope comprising:

an objective;

a field stop projection lens;

a DMD (Digital Micromirror Device) element placed perpendicularly to a specimen conjugation position and an optical axis formed with the objective;

a reflection member placed in at least one of the front and the rear on the optical axis of the DMD;

an LED light source; and

a controller to control the DMD element and the LED light source.

3) A microscope comprising:

an objective;

a field stop projection lens;

a DMD element placed perpendicularly to a specimen conjugation position and an optical axis formed with the objective;

reflection members at least each one of which is placed in the rear of the two optical axes corresponding to ON/OFF of the DMD;

shutters placed on the two optical axes, for shielding rays of an illumination light path; and

a controller to control the DMD element and the shutters.

4) The microscope according to claim 1 or 3, wherein control to open the shutter after control of the DMD element is performed simultaneously with the illumination.

5) The microscope according to claim 2, wherein control to light the LED after control of the DMD element is performed simultaneously with the illumination.

3. Field of the Invention, Prior Art

(Our company's technique)

1. Japanese Patent Application No. 2001-304123

(Other company's technique)

1. Jpn. Pat. Appln. KOKAI Publication No. 7-134250 (NIKON)

2. Jpn. Pat. Appln. KOKAI Publication No. 2000-502472 (LEICA)

The present invention relates to a microscope, and particularly to an illumination device for a fluorescent

microscope.

As shown in the Japanese Patent Application No. 2001-304123, there has been proposed an illuminating device for a microscope with Koehler's illumination, in which the DMD (Digital Micromirror Device) element is arranged at a specimen conjugation position.

4. Problem to be Solved by the Invention (Object of the Invention)

Generally, a protection glass is necessary for the DMD element to protect micromirrors because of its structure, and the protection glass is arranged adjacent to the micromirrors. Further, there exist gaps between the micromirrors although the gaps are minute.

Then, when the rays of illumination light are made incident to the DMD element, rays of reflected light from these protection glasses or the gaps of the micromirrors exist as rays of stray light without depending on control of the micromirrors, although the rays of stray light are very weak.

When using it as an illumination optical system in this condition, for instance, in the case where the rays of illumination light are intended to illuminate only part of a specimen by control of the micromirrors, the rays of illumination light (the rays of stray light) are also irradiated to outside a specified area although the rays of illumination light (the rays of stray light) are slightly irradiated.

In the case where an object of area designation is not to illuminate additional light to the specimen other than the

specified portion for the purpose of specimen protection, effect of the specimen protection is impaired because the slight rays of illumination light are irradiated to the entire specimen.

Further, in the case where an object of area designation is partial discoloration of a fluorescent label by FRAP and the like, since the rays of illumination light for discoloration are always irradiated by the rays of stray light to the entire specimen, discoloration frequently occurs in the entire specimen, particularly when illumination time is long. Therefore, there is a possibility that contrast degrades, in such a case where diffusion is observed while performing fluorescent observation with respect to the entire specimen after actual discoloration control.

5. Means for Solving the Problem and Function

The present invention is provided with a shutter opened and closed in conjunction with control of the DMD element in an illumination light path, so that the rays of illumination light are not irradiated to a specimen other than time for control of the DMD element by opening and closing the shutter in accordance with the control of the DMD element from the computer.

Further, the rays of illumination light are not irradiated to the specimen other than time for control of the DMD element by turning the LED light source ON/OFF in conjunction with control of the DMD element.

6. Embodiments of the Invention

(First Embodiment)

FIG. 1 is a view showing a first embodiment of the present invention, and shows a schematic optical view of a microscope optical system.

Reference numeral 1 denotes a light source such as a mercury lamp. 2 denotes a collimator. 3 denotes a reflection mirror. 4 denotes a DMD (Digital Micromirror Device) element. 5 denotes a field stop projection lens. 6 denotes an excitation filter selectively transmitting rays of illumination light from the light source. 7 denotes a dichroic mirror. 8 denotes an objective. 9 denotes a fluorescent specimen. 10 denotes an absorption filter selectively transmitting fluorescence from the specimen 9. 11 denotes an imaging lens. 12 denotes a prism. 13 denotes an eyepiece lens. 14 denotes an observation optical axis composed of the objective 8, and 15 denotes an illumination optical axis formed in such a way that the observation optical axis is reflected by the dichroic mirror 7. 16 denotes a high speed shutter capable of shielding the rays of illumination light. 16' denotes another arrangement example of the high speed shutter 16. 17 denotes a camera for obtaining an observation image. 18 denotes a computer for controlling image processing, the DMD element and control of the shutter. 19 denotes a monitor connected to the computer. 20 denotes a drive controller for performing driving control of the DMD element and the shutter under the control of the computer 18.

The DMD element 4 is arranged so as to be perpendicular to the illumination optical axis 15, so that rays of light are

made to be projected perpendicularly to the observation optical axis 14. Further, the DMD element 4 is composed of micromirrors 4a, 4b, ··· (only two elements are illustrated. Practically, the micromirrors have arrangement of, for instance, 1024 × 768 pieces), and the micromirrors can be inclined individually in a stable fixed state at a predetermined inclination angle ± α to each perpendicular line. The inclination angle α depends on the DMD used, which is, for instance, $\alpha = 10°$. Further, each micromirror has a predetermined area depending on the DMD, and, for instance, a square of 20 μm or less. Each micromirror can be switched between fixed states with response speed of 10 μ sec order. The fixed state is called "ON" state in which rays of light from the light source 1 are led in the direction of the illumination optical axis 15, and on the other hand, the fixed state is also called "OFF" state in which rays of light from the light source 1 are led in the direction of the other optical axis 21.

A focal position of the projection lens 5 is arranged so as to come to a pupil position of the objective 8 and a position on the surface of the DMD element 4.

An operation of the device constituted as above will be described below.

The rays of light emitted from the light source 1 and converged by the collimator 2 are reflected by the reflection mirror 3 to be led to the DMD 4, when the shutter 16 opens. In portions (for instance, 4a) where the micromirrors on the DMD 4 are ON, the rays of light are reflected in the direction of

the illumination optical axis 15 to be led to the projection lens 5. In portions (for instance, 4b) where the micromirrors on the DMD 4 are OFF, the rays of light are reflected in the direction of a retreating optical axis 21 to be not used as illumination. The rays of light led by the projection lens 5 are selected so as to be the rays of light suitable for excitation of a fluorescent material of the specimen 9 by the excitation filter 6, reflected by the dichroic mirror 7, and irradiated to the specimen 9 by the objective 8. Fluorescence emitted from the specimen 9 is converged by the objective 8, and passes through the dichroic mirror 7. The fluorescence having transmitted through the dichroic mirror 7 is selectively transmitted by the absorption filter 10. The fluorescence having transmitted through the absorption filter 10 is image-formed by the image formation lens 11, deflected by the prism 12, and observed by the eyepiece 13. Here, images of the respective micromirrors of the DMD element 4 are formed on a focus plane of the specimen 9 by the field stop projection lens 5 and the objective 8. Images of the micromirrors 4a are brightly projected since the reflected lights are led to the surface of the specimen 9. On the other hand, images of the micromirrors 4b are very darkly projected since the reflected light is not led to the surface of the specimen 9. That is, the images of the respective micromirrors of the DMD element 4 are projected onto the specimen 9 as bright and dark in accordance with the state of "ON" and "OFF". Therefore, only parts corresponding to bright are illuminated. In this manner,

partial illumination is enabled based on the "ON" and "OFF" control of the respective micromirrors of the DMD.

For instance, FIG. 2B is a view showing control state of the DMD element 4, in which only the micromirrors corresponding to an area 31 specified on a screen of the monitor 19 as shown in FIG. 2A become "ON" state. FIG. 2C shows a state that FIG. 2C is projected on a specimen surface, the area 33 corresponds to the area 32 on the DMD element 4, and only part of the area 33 comes to be illuminated brightly to an observation visual field 34. Further, it is possible to illuminate the areas 33a, 33b and 33c independently of each other and it is possible to sequentially illuminate the areas 33a, 33b and 33c with high speed switching by controlling the DMD. Three portions of areas have been exemplified. However, if control is possible with the micromirror on the DMD element 4 as a minimum unit, there is no limitation in the number of areas, and its size or shape can be changed arbitrarily.

However, here, there exist the protection glass 22 and the gaps 23 of the micromirrors in the DMD element 4. Rays of reflected light 24, though these are weak, reflect from the protection glass 22 or the gaps 23. An axis of the rays of reflected light 24 does not coincide with the illumination optical axis 15, but forms a smaller angle with respect to the illumination optical axis than the retreating optical axis 21. Thus, in some cases, rays of reflected light reflected near the illumination optical axis 15 may possibly become rays of stray light and be led to the field stop projection lens 5, thereby

the rays of reflected light are led to an unintended position of the specimen 9. For instance, as described above, even in the case where the micromirrors of the area 31 are made to turn "ON" and only the area 33 is intended to be illuminated, the rays of reflected light from the protection glass 22 or the gaps 23 illuminate part other than the area 33 of the observation visual field 32.

The rays of reflected light from the protection glass 22 or the gaps 23 are much weaker than the rays of proper reflected light at the time "ON" of the micromirrors and do not lead to a problem in many cases. However, when an intensity of rays of illumination light is high or when an illumination time of illumination light is long, influence on the specimen must be taken into consideration.

For example, in general fluorescent observation, in the case where only one cell in plural cells cultured in a laboratory dish is to be selected, only part (for instance, area 33a) corresponding to the cell is illuminated. However, cells other than an observation target cell are irradiated with weak rays of illumination light due to the stray light from the protection glass 22 or the gaps 23. Thus, when the stray light is applied for a long time due to a long time observation, cells other than the observation target cell may possibly have discoloration or may be weakened in some cases.

Moreover, in the FRAP (Fluorescence Recovery after Photobleaching) observation which is means for observing substance movement within a cell in such a way as to partially

discolor a visual field at the time of fluorescent observation and to observe its restoration state, by controlling the DMD element 4, discolored area (position, shape, size) is specified and fluorescence is partially discolored while irradiating the rays of illumination light for a fixed time. After that, all micromirrors of the range corresponding to the visual field 32 of the DMD element 4 are turned "ON" to perform fluorescent observation, followed by observing diffusion of fluorescent color component of periphery to a part discolored. At this time, by the influence of the above described rays of stray light, discoloration proceeds in the entire specimen because the rays of illumination light are irradiated over the whole specimen range including a range other than a discoloration range while the light source is turned ON. Since rays of illumination light discoloring the specimen for the observation having a high intensity are applied to a range in which discoloration is performed, in some cases, discoloration caused by the stray light cannot be ignored even if it is very weak stray light. When a range other than the specified range is discolored, difference between a discoloration area and a florescent area becomes small at the time of performing the fluorescent observation of the observation visual field 32. As a result, a contrast is degraded. When the contrast is low in this manner, not only is the observation inaccurately performed, but also an observation result may not be obtained in some cases.

In the present embodiment, there is arranged the controllable shutter 16 within the illumination light path. By

controlling the shutter 16 in conjunction with control of the DMD element 4, the rays of illumination light at the time other than necessary time are interrupted, so that it becomes possible to cut specimen irradiation of the rays of illumination light caused by the rays of stray light described above as much as possible.

For instance, one example of a flow of the FRAP observation will be shown below.

- Start observation (switch ON)
- Close shutter
- Set to observation method (fluorescence, phase difference or the like) capable of confirming required portion of object sample (hereinafter, described with case of fluorescence)
- Set specimen
- Support preparation observation start
  - Turn micromirrors (DMD) full ON
  - Open shutter
  - Pick up image with camera (CCD or the like)
  - Terminate image pick-up
  - Close shutter
  - Store image
- Terminate preparation observation
- Support parameter specification start
  - Display picked-up sample image on monitor (access image)
  - Specify area to which rays of illumination light are

irradiated while confirming the area on the monitor (area specification), plural areas can be specified (Specification method is arbitrary, such as free hand specification, or specification performed in every block classified before hand)

- Store specified area in the computer (area storage)
- Select micromirrors corresponding to discoloration irradiation area with the computer while accessing stored data (access area)
- Select discoloration illumination irradiation time
- Access area storage data, specify observation area
- Specify observation time

- Terminate parameter specification
- Support application start
- Illuminate for discoloration
- Output selected discoloration area micromirror to drive controller
- Output selected discoloration illumination irradiation time to drive controller
- Drive controller turns selected micromirror ON
- Open shutter
- Irradiate discoloration illumination
- Terminate irradiation time
- Close shutter

- Observe elapse
- Output micromirrors of observation range area to drive controller

- Drive controller turns selected micromirrors ON
- Open shutter
- Pick up image with camera
- Terminate observation specification time
- Close shutter

- Terminate application
- Remove specimen
- Terminate observation

In the above described FRAP observation flowchart, the preparation observation and the application, from start due to support to termination, automatically flow in accordance with software of the computer prepared beforehand.

Here, the illumination light is irradiated to the specimen only during shutter open to shutter close of the underlined part, and it is only the minimum time necessary for the observation or the like.

In the case where the shutter does not exist, irradiation control of the illumination light is performed in such a way as to turn all of the micromirrors of the DMD OFF, and thus specimen illumination is not performed by turning all of the micromirrors OFF at the time other than irradiation time of the underlined part. However, as described above, weak rays of illumination light from the protection glass 22 or the micromirror gaps 23 are irradiated on the specimen during the entire time from specimen setting to specimen removal on the above flowchart. In particular, parameter setting time necessary for a period from preparation observation to

application start depends on human work and takes long. Therefore, not only does the specimen suffer from damage by this irradiation time, but also there is an influence on S/N ratio deterioration in the application in the later time because fluorescence discoloration of the entire specimen occurs.

Further, as the above described flowchart, the illumination irradiation time for the specimen can be set to its required minimum in such a way that the preparation observation and the application observation are controlled so as to flow automatically by the software and controlled to be linked so as to open the shutter after setting the micromirrors of the DMD.

As described above, according to the present invention, since additional illumination irradiation to the specimen caused by the rays of stray light can be suppressed as much as possible, it becomes possible to perform preferable observation with a little discoloration of the specimen while making use of a characteristic of the DMD or with a little damage for the specimen, and with good contrast.

In the present embodiment, position of the shutter 16 is arranged closer to the light source 1 than the DMD element 4. However, as 16' shown by a dotted line, even if the shutter is arranged on the illumination optical axis 15 at the side of the projection lens 5 from the DMD element 4, there is no problem.

(Second embodiment)

FIG. 3 is a view showing a second embodiment, in which a configuration having the same function as the first embodiment

is indicated by the same number, to omit its description.

Reference numeral 41 denotes an LED light source in which "ON" (lighting)/"OFF" (lights-out) can be performed in high speed under the control of an LED drive controller. By controlling ON/OFF of the LED 41 in conjunction with control of the DMD element 4, the rays of illumination light at the time other than necessary time are interrupted, so that it becomes possible to cut specimen irradiation of illumination light caused by the rays of stray light described above as much as possible.

Like the first embodiment, a description will now be given as to a flow of observation when performing FRAP observation as follows.

- Start observation (switch ON)
- Turn LED light source OFF (confirmation)
- Set to observation method (fluorescence, phase difference or the like) capable of confirming required portion of object sample (hereinafter, described with fluorescence)
- Set specimen
- Support preparation observation start
  - Turn micromirrors (DMD) full ON
  - Turn LED light source ON
  - Pick up image with camera (CCD or the like)
  - Terminate image pick-up
  - Turn LED light source OFF
  - Store image
- Terminate preparation observation

• Support parameter specification start

• Display picked-up sample image on a monitor (access image)

• Specify area to which rays of illumination light are irradiated while confirming the area on the monitor (area specification) plural areas can be specified
(Specification method is arbitrary, such as free hand specification, or specification performed in every block classified before hand)

• Store specified area in the computer (area storage)

• Select micromirrors corresponding to discoloration irradiation area with the computer while accessing stored data (access area)

• Select discoloration illumination irradiation time

• Access area storage data, and specify observation area

• Specify observation time

• Terminate parameter specification

• Support application start

• Illuminate for discoloration

• Output selected discoloration area of micromirrors to drive controller

• Output selected discoloration illumination irradiation time to drive controller

• Drive controller turns selected micromirrors ON

• Turn LED light source ON

• Irradiate discoloration illumination

• Terminate irradiation time

- Turn LED light source OFF
- Observe elapse
- Output micromirrors of observation range area to drive controller
- Drive controller turns selected micromirrors ON
- Turn LED light source ON
- Pick up image with camera
- Terminate observation specification time
- Turn LED light source OFF
- Terminate application
- Remove specimen
- Terminate observation

In the above described FRAP observation flowchart, the preparation observation and the application, from start by support to termination, automatically flow in accordance with software of the computer prepared beforehand.

Here, the rays of illumination light are irradiated only during LED light source ON to LED light source OFF of the underlined part, and it is only the minimum time necessary for the observation or the like.

Further, as the above-described flowchart, the illumination irradiation time for the specimen can be set to its required minimum in such a way that the preparation observation and the application observation are controlled so as to flow automatically by the software and controlled to be linked so as to turn the LED light source ON after setting the micromirrors of the DMD.

As described above, according to the present invention, since additional illumination irradiation to the specimen caused by the rays of stray light can be suppressed as much as possible, it becomes possible to perform preferable observation with a little discoloration of the specimen while making use of a characteristic of the DMD or with a little damage for the specimen, and with good contrast.

Further, ON/OFF of the LED that is generally possible with several hundreds nano seconds order, coupled with high speed switching of the DMD that is possible with several tens nano seconds order, makes it possible to switch illumination portion with extremely high speed. Therefore, it becomes possible to perform observation with little influence of time lag on change of the specimen while shifting to elapse observation from the discoloration illumination.

(Third embodiment)

FIG. 4 is a view showing a third embodiment, in which a configuration having the same function and operation as the first and second embodiments is indicated by the same number, to omit its description.

Reference numerals 51, 52 denote light sources such as mercury lamps. 53, 54 denote collimators. 55, 56 denote reflection mirrors. 57, 58 denote excitation filters each of which has different characteristic. 59 denotes a reflection optical axis at the condition where the micromirrors of the DMD element 4 are ON, namely at the condition of 4a. 60 denotes a reflection optical axis at the condition where the

micromirrors of the DMD element 4 are OFF, namely at the condition of 4b. 61, 62 denote high speed shutters capable of interrupting the rays of illumination light.

There will be described operation in the microscope constituted as above.

The rays of light emitted from the light source 51 are converged by the collimator 53, selectively transmitted by the excitation filter 57 in the case where the shutter 61 is opened, and led to the DMD 4 while being reflected by the reflection mirror 55. In portions 4a of the state where the micromirrors on the DMD 4 are turned ON, the rays of light are led to the projection lens 5 while being reflected in the direction of the illumination optical axis 15. In portions 4b of the state where the micromirrors on the DMD 4 are turned OFF, the rays of light are reflected in the direction of a retreating optical axis, and not used as the illumination. Similarly, the rays of light emitted from the light source 52 are converged by the collimator 54, transmitted selectively by the excitation filter 58 when the shutter 62 opens, and led to the DMD 4 while being reflected by the reflection mirror 56. In portions of the state 4b where the micromirrors on the DMD 4 are turned OFF, the rays of light are led to the projection lens 5 while being reflected in the direction of the illumination optical axis 15. In portions of the state 4a where the micromirrors on the DMD 4 are turned ON, the rays of light are not used as the illumination while being reflected in the direction of the retreating optical axis.

Here, in the FRAP observation described in the first and

second embodiments, in order to perform discoloration in as short a time as possible, there is performed increase of energy while shortening (for instance using UV) wavelength of the illumination used in the discoloration, or increase of energy while using a light source with a high output different from the light source for the observation. That is, in FIG. 4, the light source 51 and the excitation filter 57 are set to the characteristic suitable for the observation, while the light source 52 and the excitation filter 58 are set to the characteristic suitable for the specimen discoloration.

In the device set as above, like the first embodiment, there will be shown one example of flowchart of the FRAP observation.

- Start observation (switch ON)
- Close shutters 61, 62
- Set to observation method (fluorescence, phase difference or the like) capable of confirming required portion of object sample (hereinafter, described with fluorescence)
- Set specimen
- Support preparation observation start
  - Turn micromirrors (DMD) full ON
  - Open shutter 61
  - Pick up image with camera (CCD or the like)
  - Terminate image pick-up
  - Close shutter 61
  - Store image
- Terminate preparation observation

• Support parameter specification start

• Display picked-up sample image on a monitor (access image)

• Specify area to which rays of illumination light are irradiated while confirming the area on the monitor (area specification) plural areas can be specified (Specification method is arbitrary, such as free hand specification, or specification performed in every block classified before hand)

• Store specified area in the computer (area storage)

• Select micromirrors corresponding to discoloration irradiation area with the computer while accessing stored data (access area)

• Select discoloration illumination irradiation time

• Access area storage data, and specify observation area

• Specify observation time

• Terminate parameter specification

• Support application start

• Illuminate for discoloration

• Output selected discoloration area of micromirrors to drive controller

• Output selected discoloration illumination irradiation time to drive controller

• Drive controller turns selected micromirror OFF (others ON)

• Open shutter 62

• Irradiate discoloration illumination

- Terminate irradiation time
- Close shutter 62
- Observe elapse
- Output micromirrors of observation range area to drive controller
- Drive controller turns selected micromirrors ON (others OFF)
- Open shutter 61
- Pick up image with camera
- Terminate observation specification time
- Close shutter 61
- Terminate application
- Remove specimen
- Terminate observation

In the above described FRAP observation flowchart, the preparation observation and the application, from start due to support to termination, automatically flow in accordance with software of the computer prepared beforehand.

Here, the rays of illumination light are irradiated only during shutter open to shutter close of the underlined part, and it is only the minimum time necessary for the observation or the like.

In the configuration of the present embodiment, when the shutters 61 and 62 do not exist, the illumination from either one of the light sources is always irradiated to the specimen, and thus damage or fluorescence discoloration for the specimen cannot be avoided.

As described above, according to the present invention, due to different light source or wavelength, it is possible to perform efficient illumination while making use of respective characteristics, and to suppress additional illumination irradiation for the specimen caused by the rays of stray light as much as possible. Therefore, it becomes possible to perform discoloration for the specimen making use of characteristics of the DMD, and to perform preferable observation in which damage to the specimen is little, and contrast is good.

(Modified example 1)

Although there has been mainly described about FRAP observation in the third embodiment, it is, of course, possible to perform observation by two-color illumination with characteristic of the excitation filters 57, 58 changed.

At this time, for instance, an arbitrary area 33 corresponding to a state where the DMD element 4 within the visual field 34 of FIG. 2 is turned ON is irradiated by the rays of illumination light from the light source 51, while an area other than the area 33 corresponding to a state where the DMD element 4 is turned OFF is irradiated by the rays of illumination light from the light source 52. At this time, it is possible to illuminate the area 33 and the area other than the area 33 with different wavelengths by substituting band pass filters with different wavelength bands for the excitation filters 57, 58.

In the case of performing observation based on caged fluorescent reagent with such configuration, it is possible to

observe a state of diffusion without time lag at the same time the caged removal is performed, by illuminating the area 33 with wavelength of the caged removal, and illuminating the area other than the area 33 with wavelength of fluorescent observation after removal.

(Modified example 2)

Although the light sources 51, 52 and the shutters 61, 62 are used in the third embodiment, it is possible to obtain exactly the same effect as the third embodiment, by substituting the LED light source for a half one side of an optical path, for instance, the light source 51 at the side of the optical axis 59 to abandon the shutter 61, and by controlling ON/OFF of the LED light source instead of open/close control of the shutter 61.

Of course, it is also possible to abandon the shutters 61, 62 by substituting the LED light sources for both the light sources 51, 52.

7. Advantage of the Invention

Claim 1: embodiment 1

Claim 2: embodiment 2

Claim 3: embodiment 3

FIG. 1

17 Camera

18 Computer

19 Monitor

20 Drive controller

4a ON

4b OFF

FIG. 3

17 Camera

18 Computer

19 Monitor

20 Drive controller

42 LED drive controller

FIG. 4

17 Camera

18 Computer

19 Monitor

20 Drive controller

Support for claims in English Language Written Proposal of Invention and in the Drawings in the Japanese Language Written Proposal of Invention

16. A microscope comprising:

a light source which illuminates a specimen **(page 5, lines 1-2; page 6, line 23 to page 7, line 9)**;

an objective located opposite to the specimen **(page 5, lines 10-11; page 7, lines 9-10; Fig. 1)**;

a field stop projection lens, located on an illumination axis between the light source and the objective, to narrow a field of view of the specimen **(page 5, line 8; Fig. 1)**;

a digital micromirror device **(page 5, line 7)** which is conjugate with the specimen via the field stop projection lens and the objective **(page 6, lines 18-20; page 7, lines 16-19; claim 1)**, and which comprises a plurality of two-dimensionally arrayed micromirrors that are individually selectable to be turned on so as to reflect light along the illumination axis to the specimen **(page 5, line 26 to page 6, line 17; page 6, line 25 to page 7, line 5; page 7, line 16 to page 8, line 17)**;

a reflection mirror which reflects illumination light from the light source onto the digital micromirror device **(page 6, lines 23-25)**;

a shutter **(page 5, lines 17-20; page 10, line 26 to page 11, line 6; page 14, lines 20-24)**;

a dichroic mirror which is located on an observation axis of the objective so as to reflect the illumination light emitted from the light source onto the objective and to pass observation light from the objective **(page 5, lines 10 and 14-17; page 7, lines 5-16; Fig. 1)**;

an excitation filter which selectively passes light components of the illumination light that are suitable for excitation of a fluorescent material in the specimen **(page 5, lines 8-10; page 7, lines 5-8)**;

an absorption filter which selectively absorbs light components of the observation light **(page 5, lines 11-13; page 7, lines 11-13)**;

a camera located on the observation axis to pick up an observation image **(page 5, lines 20-21; page 11, line 19; page 13, line 3; Fig. 1)**;

a monitor which displays the image picked up by the camera **(page 5, lines 22-23; page 11, lines 25-26)**;

a drive controller which controls the digital micromirror device and the shutter **(page 5, lines 23-25)**; and

a computer **(page 5, lines 21-22)** which controls the drive controller, camera and monitor such that:

before picking up an image of the specimen, all of the micromirrors are turned on while the shutter is closed, and the shutter is opened to cause the illumination light to be guided to the specimen via the turned-on micromirrors, such that an image

of a part of the specimen that is located within the field of view is picked up by the camera, and wherein the shutter is closed after an image pick-up operation of the camera ends **(page 11, lines 9-21)**;

the image picked up by the camera is displayed by the monitor, an irradiation area to be irradiated with the illumination light is specified, and respective ones of the micromirrors which correspond to the specified irradiation area are specified **(page 11, line 24 to page 12, line 9)**; and

before picking up an image of the sample again, only the specified ones of the micromirrors are turned on while the shutter is closed, and the shutter is opened to cause the illumination light to be guided to the specimen via the turned-on micromirrors, such that another image of the part of the specimen that is located within the field of view is picked up by the camera, and wherein the shutter is closed after the image pick-up operation of the camera ends **(page 12, line 15 to page 13, line 5)**;

wherein when the shutter is closed, the shutter prevents stray light, from gaps between adjacent ones of the micromirrors, from reaching the specimen **(page 10, line 26 to page 11, line 7; page 8, line 18 to page 10, line 25; page 14, lines 13-19)**.

17. The microscope according to claim 16, wherein the shutter is located between the light source and the reflection mirror **(page 6, lines 23-25; Fig. 1)**.

18. The microscope according to claim 16, wherein the shutter is located between the digital micromirror device and the field stop projection lens **(page 14, lines 20-24)**.

19. A microscope comprising:

a light source which illuminates a specimen **(page 5, lines 1-2; page 6, line 23 to page 7, line 9)**;

an objective located opposite to the specimen **(page 5, lines 10-11; page 7, lines 9-10; Fig. 1)**;

a field stop projection lens, located on an illumination axis between the light source and the objective, to narrow a field of view of the specimen **(page 5, line 8; Fig. 1)**;

a digital micromirror device **(page 5, line 7)** which is conjugate with the specimen via the field stop projection lens and the objective **(page 6, lines 18-20; page 7, lines 16-19; claim 1)**, and which comprises a plurality of two-dimensionally arrayed micromirrors that are individually selectable to be turned on so as to reflect light along the illumination axis to the specimen **(page 5, line 26 to page 6, line 17; page 6, line 25 to page 7, line 5; page 7, line 16 to page 8, line 17)**;

a reflection mirror which reflects illumination light from the light source onto the digital micromirror device **(page 6, lines 23-25)**;

a shutter **(page 5, lines 17-20; page 10, line 26 to page 11, line 6; page 14, lines 20-24)**;

a dichroic mirror, which is located on an observation axis of the objective so as to reflect the illumination light emitted from the light source onto the objective and to pass observation light from the objective **(page 5, lines 10 and 14-17; page 7, lines 5-16; Fig. 1)**;

an excitation filter, which selectively passes light components of the illumination light that are suitable for excitation of a fluorescent material in the specimen **(page 5, lines 8-10; page 7, lines 5-8)**;

an absorption filter which selectively absorbs light components of the observation light **(page 5, lines 11-13; page 7, lines 11-13)**;

a camera located on the observation axis to pick up an observation image **(page 5, lines 20-21; page 11, line 19; page 13, line 3; Fig. 1)**;

a drive controller which controls the digital micromirror device and the shutter **(page 5, lines 23-25)**; and

a computer **(page 5, lines 21-22)** which controls the drive controller such that:

before picking up an image of the specimen, desired ones of the micromirrors are turned on while the shutter is closed, and the shutter is opened to cause the illumination light to be guided to the specimen via the turned-on micromirrors, and wherein the shutter is closed after an image pick-up operation of the camera ends, **(page 12, line 15 to page 13, line 5)** so as to prevent stray light, from gaps between adjacent ones of the micromirrors, from reaching the specimen **(page 10, line 26 to page 11, line 7; page 8, line 18 to page 10, line 25; page 32, lines 13-19)**.

20. The microscope according to claim 19, wherein the shutter is located between the light source and the reflection mirror **(page 6, lines 23-25; Fig. 1)**.

21. The microscope according to claim 19, wherein the shutter is located between the digital micromirror device and the field stop projection lens **(page 14, lines 20-24)**.